Estimates of the health effects of air pollution are alarming, with up to 7 million attributable deaths worldwide each year. Although the pulmonary effects of air pollution are widely recognized, it is only in the last few decades that the adverse cardiovascular effects of air pollution have become apparent. Exposures to diesel exhaust, a prominent source of urban air pollution and a pollutant rich in combustion-derived nanoparticles, has multiple detrimental actions on the cardiovascular system. Brief exposure to diesel exhaust at concentrations encountered at the roadside of heavily polluted cities promotes vasoconstriction, causes impaired relaxation of blood vessels, increases arterial stiffening, promotes blood clotting, inhibits the release of fibrinolytic factors, and promotes myocardial ischemia. Parallel animal studies have shown that diesel exhaust particles also generate free radicals, increase blood pressure, promote atherosclerosis, induce arrhythmia, and increase the susceptibility of the heart to injury (Figure). The current findings seem to contradict these earlier observations. The authors suggest that the seemingly opposing effects of roadside proximity, and therefore exposure to traffic-derived air pollutants, with those of ambient PM exposure is resolved by noting that roadside proximity was associated with an increase in distinct CD133+ and CD31+ cell populations, but not those specific populations that were decreased by PM1.3 exposure in their earlier study. It is perhaps premature though to suggest that the effects of exposure to road traffic and PM, are mediated through different progenitor cell subpopulations, given we have only a limited understanding of the role for these cell populations even in studies that have evaluated their response to direct vascular injury. Indeed, there is an urgent need to evaluate which of these phenotypic subpopulations make a meaningful contribution to vascular repair. Although it is clear that endothelial outgrowth can be obtained from circulating mononuclear cells, the origin and precise phenotype of their precursor remains uncertain.

It is interesting that of the 15 cell populations evaluated, the associations with roadway proximity were strongest for 2 of the more abundant cell types: those that expressed the stem cell marker CD133 and those that coexpress CD133 with the endothelial cell marker CD31. This may reflect the challenges of accurately enumerating rare subpopulations in blood where, for example, the levels of CD31+CD45+CD133+ cells were 100-fold lower than those of the parent CD31 population. Irrespective of this methodological challenge, the association between roadside proximity and circulating angiogenic cells was strongest for CD133+CD31+ cells. Endothelial progenitor cells in culture begin to lose CD133 and start to express mature endothelial cell markers CD31, VE-cadherin, and von Willebrand Factor, suggesting that the CD133+CD31+ cells influenced by road traffic exposure may be an important population of endothelial progenitor cells in transition.

This paradox between the different responses to roadside proximity or estimates of urban PM exposure also highlights another major concern in this field—that environmental monitoring of PM pollution in public places may be overlooking the key pollutants linked to health effects. PM is measured gravimetrically using stationary monitors, but these gravimetric measures are skewed by larger particles. Vehicle exhausts are especially rich in combustion-derived nanoparticles (diameter <0.1 μm). These particles have an extremely large reactive surface area for a relatively small mass, readily deposit deep into the alveoli, and may even access the circulation to directly damage the cardiovascular system. Together with the often distant location of many stationary monitors from the source of such particles (road vehicles), the risks associated with combustion-derived nanoparticles are under-represented or, as the present study may demonstrate, obfuscated by the generalization of air pollutants.

Road Repairs
Does Exposure to Traffic Affect Mechanisms of Vascular Injury and Repair?

Mark R. Miller, Nicholas L. Mills, David E. Newby

In this edition of the journal, DeJarnett et al elaborate on another potentially important mechanism through which traffic-derived air pollution could promote cardiovascular disease. The authors studied 316 individuals with cardiovascular risk factors and examined whether angiogenic cells in blood are related to the proximity of their residence to major roadways. The investigators demonstrate that volunteers living within 300 m of a major road have higher numbers of circulating cells with characteristics of early stem cells and vascular endothelial cells. The association was not linked to evidence of a systemic inflammatory response. The thoroughness of the study design is commendable: using a large sample group for the degree of cell profiling (15 different cell populations), detailed evaluation of roadside proximity and traffic density, and accounting for multiple potential confounding variables, including cigarette smoking and socioeconomic factors.

The present study expands on their earlier findings, whereby exposure to fine particulate matter (PM1.3) during a high air pollution episode was associated with a decrease in circulating progenitor cells. The current findings seem to contradict these earlier observations. The authors suggest that the seemingly opposing effects of roadside proximity, and therefore exposure to traffic-derived air pollutants, with those of ambient PM exposure is resolved by noting that roadside proximity was associated with an increase in distinct CD133+ and CD31+ cell populations, but not those specific populations that were decreased by PM1.3 exposure in their earlier study. It is perhaps premature though to suggest that the effects of exposure to road traffic and PM, are mediated through different progenitor cell subpopulations, given we have only a limited understanding of the role for these cell populations even in studies that have evaluated their response to direct vascular injury. Indeed, there is an urgent need to evaluate which of these phenotypic subpopulations make a meaningful contribution to vascular repair. Although it is clear that endothelial outgrowth can be obtained from circulating mononuclear cells, the origin and precise phenotype of their precursor remains uncertain.

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DeJarnett et al\textsuperscript{16} raise an important limitation of the study, that the design does not assess exposure on an individual level. Potential exposure to traffic-related pollutants was based on the location of the volunteers’ residential address and did not account for time spent in this residence or activity when not at this location. These factors influence not only total exposure, but also exposure to specific pollutants and the dose rate of exposure. Subsequent studies could consider personal exposure to PM through the use of portable PM monitoring devices\textsuperscript{23,24} that are evolving to provide greater reliability, better stratification of particle size distributions, and sampling of particulates for toxicological studies. Ultimately, controlled human exposure studies and experimental studies are necessary to demonstrate causality and to understand the functional consequences of exposure on circulating progenitor cells. However, if the current observations are verified, then it would suggest that our daily exposure to traffic-derived air pollutants not only results in vascular injury, but may also affect our capacity to repair the cardiovascular system.

Despite improvements in air quality over the last few decades, air pollution remains a burgeoning public health issue that demands greater attention to ensure effective regulation. Programmes of funding that bring together multiple disciplines (epidemiologists, exposure scientists and modellers, physicians and toxicologists) will be vital to accurately address which air pollutants are responsible for each aspect of their pathophysiological actions. Such harmonization of research aims will better identify susceptible groups, refine current monitoring strategies, and support the implementation of effective public health policy to tackle air pollution.

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Disclosures
None.

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